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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/263,626	03/05/1999	PAUL A. MOORE	PF466	2059

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EXAMINER	
BRANNOCK, MICHAEL T	
ART UNIT	**PAPER NUMBER**
1646	

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.	Applicant(s)
09/263,626	P.A. Moore et al.
Examiner	**Art Unit**
Michael Brannock, Ph.D	1646

– The MAILING DATE of this communication appears on the cover sheet with the correspondence address –

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on *Oct 15, 2002*

2a) ☐ This action is **FINAL.** 2b) ☒ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) *25-50, 60-131, and 133-151* is/are pending in the applica

4a) Of the above, claim(s) _____ is/are withdrawn from considera

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) *25-50, 60-131, and 133-151* is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirem

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are a) ☐ accepted or b) ☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____ .
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

a) ☐ The translation of the foreign language provisional application has been received.

15) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☑ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s). 25
4) ☐ Interview Summary (PTO-413) Paper No(s). _____
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

Response to Amendment

1. The request filed on 7/30/02 for a Continued Prosecution Application (CPA) under 37 CFR 1.53(d) based on parent Application No. 09263626 is acceptable and a CPA has been established. An action on the CPA follows.

Maintained Rejections:

2. Claims 25-50, 61-131 and 133-151 stand rejected 35 U.S.C. § 112 first paragraph, as set forth in item 3 of Paper 22, 4/22/02, in item 7 of Paper 15, and as set forth in item 7, beginning at the second paragraph, and in item 10 of Paper 11 (8/29/00). Specifically, because the claims are not enabled in their full scope, i.e. the specification, while being enabling for a polynucleotide encoding a polypeptide of SEQ ID NO: 2 and for polypeptides consisting of fragments of SEQ ID NO: 2, and for polynucleotides that specifically hybridize to a polynucleotide of SEQ ID NO: 1, does not provide enablement for polynucleotides comprising only portions of SEQ ID NO: 1 nor for polynucleotides encoding polypeptides that comprise only portions of SEQ ID NO: 2 or have any recited degree of homology to SEQ ID NO: 2.

As set forth above, assuming that one skilled in the art would understand that the instant receptor is expressed in activated T-cells as opposed to resting T-cells, then it is reasonable to also assume that one of skill in the art could use polynucleotides of SEQ ID NO: 1 as hybridization probes to detect activation of T-cells. Similarly, it is reasonable to assume that the

skilled artisan could use the polypeptides of SEQ ID NO: 2 to raise antibodies useful for the detection and/or isolation of activated T-cells. However, the claims encompass a virtually limitless number of polynucleotide variants of SEQ ID NO: 1. It is reasonable to assume that many of the encompassed polynucleotides could be used as hybridization probes that are specific to SEQ ID NO: 1 such that detection of activated T-cells could be achieved, yet the claims are not so limited to hybridization probes and the specification has failed to teach how to use other claimed polynucleotides that could not be used as probes for SEQ ID NO: 1. Of those polynucleotides that may not be useful as probes, it can be expected that only a small number will encode a polypeptide of SEQ ID NO: 2 due to the degeneracy of the genetic code. This small number is enabled. However, polynucleotides encoding variants of SEQ ID NO: 2 are not enabled, as set forth previously, particularly at page 6 of Paper 6 (1/3/00) and on page 8 of Paper 11 (8/29/02). Applicant's arguments regarding enablement for polynucleotide variants of SEQ ID NO: 1 have been substantially addressed previously in Papers 6 and 11.

Applicant additionally argues that polynucleotides encoding polypeptide variants of SEQ ID NO: 2 would be useful for generating antibodies or other antagonists of SEQ ID NO: 2. This argument has been fully considered but not deemed persuasive. The specification has provided little or no guidance beyond the mere presentation of sequence data to enable one of ordinary skill in the art to determine, without undue experimentation, the positions in the protein which are tolerant to change (e.g. such as by amino acid substitutions or deletions), and the nature and extent of changes that can be made in these positions to effect or retain any particular property.

These or other regions may also be critical determinants of antigenicity. It is well appreciated in the art of antibody production that it is unpredictable which amino acids are critical antigenic determinants (see Alexander et al., Proc. Natl. Acad. Sci. 89(3352-3356)1992. Protein antigenicity can be significantly reduced by substitution of even a single residue. Further, even if an amino acid substitution does not destroy the activity of the immunizing protein, the substitution may significantly reduce the antigenicity of the protein (see the Abstract of Alexander et al.). The specification does not provide sufficient guidance as to how to make antibodies that are specific to variants of SEQ ID NO: 2 that can be used for any specific purpose. The specification has not provided guidance as to natural variants that may exist, nor how to use antibodies specific to variants that might be created.

3. Claims 140-155 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention, as set forth previously in item 4 of Paper 22 and in item 12 of Paper 6 regarding claim 51, and reiterated below.

The claims require a polynucleotide encoding a polypeptide of SEQ ID NO: 2 named Cytokine Receptor Common Gamma Chain Like (CRCGCL) wherein the polypeptide regulates the differentiation and or proliferation of immune cells. The specification discloses that CRCGCL shares homology with members of the cytokine receptor family (see page 1, lines 8-9)

and that binding of a cytokine to members of this family stimulates certain and often independent signal transduction pathways (lines 19-20); and also, that members of this family regulate a variety of cellular process, including activation, proliferation, and differentiation (lines 21-23) of such cell types as T and B lymphocytes, natural killer cells, macrophages and monocytes (lines 26-28). The specification also provides guidance to one skilled in the art to try various experiments through which the activity (if any) of CRCGCL on specific cell types might then be determined (e.g. see Examples 15, 16 and 17: pages 90-94). These suggested experiments, however, provide the skilled artisan with only a starting point for further research and investigation. The specification has failed to teach one of skill in the art which cell types to use, if any can be used, to regulate cell differentiation and/or proliferation with CRCGCL. Furthermore, if certain cell types can be regulated with the claimed invention, then the specification has not provided guidance as to the nature of the regulation, e.g. the specification has not taught whether to use CRCGCL to promote or to inhibit cell differentiation and/or proliferation. Furthermore, the specification puts forth that the closest homolog of CRCGCL is the Interleukin-2 receptor gamma (see page 2, lines 27-29). R.E. Callard and A.J.H. Gearing (The Cytokine FactsBook, Academic Press, London 1994) teach that the IL-2 receptor gamma does not bind cytokine directly, but works in conjunction with IL-2 receptor alpha and or beta subunits (see page 41, line 4). The specification asserts that CRCGCL binds to cytokines but does not provide evidence to support the assertion, therefore, absent evidence to the contrary,

CRCGCL (alone) would not be expected to regulate the differentiation and/or proliferation of cells as is required by claims 140-155.

Applicant argues that the specification teaches that the "proliferation and/or differentiation" of "immune cells" can be "regulated". This argument has been fully considered but not deemed persuasive. As set forth previously, to determine which immune cells (e.g. platelets, RBCs, neutrophils, macrophages, etc.) could be regulated and then to determine the nature of the regulation, e.g. chemotaxis, increase/decrease in proliferation, increase/decrease in differentiation, etc., would be unduly burdensome, as one highly skilled in the art would immediately appreciate. The specification has provided nothing more than an invitation to begin this extensive, random trial and error experimentation.

Applicant argues that the Declaration of Thi-Sau Migone (Paper 20) under 37 CFR 1.132 filed 2/14/02 and the specification particularly at page 56 clearly establish that the specification asserts that the polypeptides can be used to increase proliferation of specific cell types. This argument has been fully considered but not deemed persuasive. At pages 56-62 the specification simply makes generalized statements regarding any potential activity of the polypeptides toward any number of immune cell types. Statements such as "CRCGCL polynucleotides or polypeptides may have chemotaxis activity" Page 61 line 21, for example, do not provide the artisan with any particular knowledge, - only that the polypeptides might be tested for such activities.

Finally, Applicant agues that the examiner's assertion that it is unlikely that the instant SEQ ID NO: 2 is capable, alone, of binding a cytokine is misplaced. This argument has been fully considered but not deemed persuasive. As set forth above, the specification puts forth that the closest homolog of CRCGCL is the Interleukin-2 receptor gamma (see page 2, lines 27-29). R.E. Callard and A.J.H. Gearing (The Cytokine FactsBook, Academic Press, London 1994) teach that the IL-2 receptor gamma does not bind cytokine directly, but works in conjunction with IL-2 receptor alpha and or beta subunits (see page 41, line 4). The specification asserts that CRCGCL binds to cytokines but does not provide evidence to support the assertion, therefore, absent evidence to the contrary, CRCGCL (alone) would not be expected to regulate the differentiation and/or proliferation of cells as is required by claims 140-155. Thus, these facts evidence a lack of enablement regarding claims 140-155.

Applicant argues that subsequent work, e.g. Reche et al. and that provided in the Declaration of Thi-Sau Migone, demonstrate that CRCGCL binds the cytokine TSLP. This argument has been fully considered but not deemed persuasive; the issue, as reiterated above, is that CRCGCL (alone) would not be expected to regulate the differentiation and/or proliferation of cells as is required by claims 140-155. In fact, analogous to the known activity of Interleukin-2 receptor gamma which requires IL-2 receptor alpha and or beta subunits, Reche et al., teach that a functional complex involving the instant CRCGCL requires the involvement of IL-7Rα and TSLP (see page 338, col 2, Identification of a functional heteromeric human TSLP receptor complex). The instant specification says nothing about TSLP; the specification directs the

skilled artisan to search for binding of a multitude of cytokines but does not mention TSLP (see page 85, lines 20-28). Additionally, the specification does not guide the skilled artisan to use the instant polypetides in conjunction with any IL receptor alpha chain, much less provide guidance to use the IL-7Rα. Further, the specification asserts that preliminary data indicates that the instant polypeptides interact with Jak1 (see page 86, line 1) whereas the Declaration filed under 37 CFR 1.132 filed as Paper 14, 2/27/01 indicates that Jak2 is involved and says nothing about Jak1. Thus, the specification does not provide adequate guidance to produce a polypeptide of SEQ ID NO: 2 that regulates the differentiation and/or proliferation of cells as is required by claims 140-155

Thus, due to the large quantity of experimentation necessary to determine which cell types, could be used with the claimed invention and then to determine the nature of the regulation of the cells that are to be used, the absence of working examples wherein CRCGCL is used to regulate cell proliferation and/or differentiation, the complex nature of the art - e.g. R.E. Callard and A.J.H. Gearing (supra) teach that IL-2 receptor regulation occurs through multifaceted protein/protein interactions, undue experimentation would be required of the skilled artisan to use the claimed invention.

4. Claims 25-50, 60-131 and 133-155 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the

application was filed, had possession of the claimed invention, as set forth previously in item 11 of Paper 15, and reiterated below.

The specification discloses a polynucleotide of SEQ ID NO: 1, yet the claims encompass polynucleotides not described in the specification, e.g., sequences from other species, mutated sequences, allelic variants, or sequences that have a recited degree of identity. None of these sequences meet the written description provision of 35 U.S.C. 112, first paragraph. Although one of skill in the art would reasonably predict that these sequences exist, one would not be able make useful predictions as to the nucleotide positions or identities of those sequences based on the information disclosed in the specification.

With the exception of the of the polynucleotide of SEQ ID NO: 1, the skilled artisan cannot envision the detailed chemical structure of the encompassed variants. Therefore, only the polynucleotide of SEQ ID NO: 1, and polynucleotides *consisting* of fragments thereof, but not the full breadth of the claims meet the written description provision of 35 U.S.C. §112, first paragraph.

Applicant argues that any skilled artisan can readily identify every polynucleotide encoding a polypeptide having the recited % identity of SEQ ID NO: 2, and distinguish them from all others. This argument has been fully considered but not deemed persuasive. The skilled artisan readily appreciates that the claims encompass a genus, that for any practical purpose, contains an essentially limitless number of variants. Applicant's description of one such member is not sufficient to describe this practically limitless genus.

Claim Rejections - 35 USC § 102

5. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

6. Claims 140, 143, and 153 are rejected under 35 U.S.C. 102(b) as being anticipated by GenEmbl accession number X91553, as set forth in the second paragraph of item 13 of Paper 15 and reiterated below. The claims require that the claimed polynucleotide encode a fragment of SEQ ID NO: 2, wherein said fragment enhances the differentiation and/or proliferation of immune cells. The polypeptide of SEQ ID NO: 2 comprises a fragment consisting of the amino acid phenylalanine (at position 260, for example). GenEmbl accession number X91553 discloses a polynucleotide that comprises a nucleic acid sequence that encodes the amino acid phenylalanine. It is inherent feature of phenylalanine that it promotes (enhances) the proliferation of all animal cells (immune cells included) because it is an essential amino acid, see Lodish eds, Molecular Biology, page 193.

Applicants argues that one skilled in the art would not consider the effect of an essential amino acid to be equivalent to the modulation or enhancement of proliferation required by the

claims. This argument has been fully considered, addressed previously, but not deemed persuasive. Applicant additionally argues that phenylalanine does not enhance of inhibit cell growth above or below levels seen in standard culture conditions of which it is a component. This argument has been fully considered but not deemed persuasive because it basically a circular argument. Applicant is essentially arguing that phenylalanine does not enhance cell growth beyond the enhancement seen when phenylalanine is present - such an argument is not persuasive.

Conclusion

No claims are allowable.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Michael Brannock, Ph.D., whose telephone number is (703) 306-5876. The examiner can normally be reached on Mondays through Thursdays from 8:00 a.m. to 5:30 p.m. The examiner can also normally be reached on alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yvonne Eyler, Ph.D., can be reached at (703) 308-6564.

Official papers filed by fax should be directed to (703) 308-4242. Faxed draft or informal communications with the examiner should be directed to (703) 308-0294.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

MB

October 30, 2002

YVONNE EYLER, PH.D
SUPERVISORY PATENT EXAMINER
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